PhD position
Unraveling the physical mechanisms of bacterial aggregation in biofilm initiation

Context and work environment

Context: Bacteria spend most of their life attached to surfaces, in structured colonies encased in a self-produced polymeric matrix called biofilms, which are the prevalent form of life on earth. The organization in biofilms confers them a selective advantage over the individual, e.g., by increasing resistance to mechanical damage and antibiotic agents. This strongly influences the interaction of pathogens with their host. Biofilms are thus tightly linked to the rise of multidrug-resistant strains, responsible for the majority of hospital-acquired infections.

While the genetic and biochemical basis of biofilm formation is well-studied, the role of physical forces is critically underexplored. Biofilm formation requires a transition from a free-swimming lifestyle to a sessile, cooperative one via the formation of microcolonies. For bacteria without surface motility, the initiation of microcolonies, driven by substrate adhesion and cell division is clear. However, for surface-motile bacteria like *Pseudomonas aeruginosa* (PA) which move by twitching (a motility mode which involves active pili extension and retraction), the process is more complex. Despite active movement, these bacteria start to cluster into microcolonies, but how actively moving individuals transition to stationary aggregates before surface confluence is reached, is unclear.

This Ph.D. project will use theoretical modeling and numerical simulations, combined with existing experimental data on PA motility and aggregation on various surfaces, to investigate if physical effects are a dominant mechanism for aggregation or if biological phenotypic switches induced by bacterial surface adhesion are decisive.

Team description: The Ph.D. thesis will be hosted on the Grenoble campus et the Laboratory for Interdisciplinary Physics (LIPhy), which is an interdisciplinary research institute at the interface of complex and soft matter physics and life science, combining experimental, theoretical and simulation approaches on multiple scales. The Ph.D. thesis will be supervised by K. John (MC2 Team) and E. Bertin (PSM team). The MC2 team is a joint theoretical/experimental team; K. John is specialized in modeling biophysical and complex soft matter systems. E. Bertin has a background in statistical physics, he is an expert in the theory of soft and active matter, phase transitions and coarse-graining techniques. Furthermore, the Ph.D. student will be co-supervised by A. Chauvière (BCM team) at the TIMC in Grenoble, who is specialized in modeling of living systems. Experiments on bacterial motility, which form the starting point for this theoretical Ph.D. project are conducted in the MC2 team at the LIPhy under the supervision of D. Débarre and in the Matter and Complexity team at the LPENS Lyon under the supervision of S. Lecuyer.

Other academic partners: The Ph.D. thesis will be integrated into the German-French doctoral school "Living Fluids" between Grenoble, Saarbrücken, Bayreuth, Münster and Rabat. The doctoral school also provides a framework for a possible 2-month visit in one of the partner groups of the network. The group of Prof. U. Thiele at the Univ. Münster would be the ideal place for the analysis of a coarse-grained model using parameter continuation techniques.

Unraveling the physical mechanisms of bacterial aggregation in biofilm initiation

Description of the project: Bacteria predominantly thrive in biofilms—structured communities that confer major advantages, including increased antibiotic resistance. While the genetic and biochemical basis of biofilm formation is well-studied, the role of physical forces is critically underexplored. This project investigates the initiation of biofilms by surface-motile bacteria like Pseudomonas aeruginosa (PA). These actively moving individuals must transition to stationary microcolonies, and the mechanism driving this aggregation remains unclear. We will test the hypothesis that Motility Induced Phase Separation (MIPS) is a dominant mechanism for microcolony initiation. MIPS is an active matter phenomenon where the local slow-down of bacterial movement, caused by increased density (e.g., from collisions or local signaling), creates a positive feedback loop that drives clustering, even in the absence of attractive chemical forces. This research will combine theoretical modeling and numerical simulations with existing experimental data on PA to determine if MIPS is the primary driver of aggregation or if biological factors, such as adhesion-induced phenotypic switches, are more decisive. Understanding this physical transition is key to developing novel strategies to combat multidrug resistance.

Possible research axes:

1. The Ph.D. candidate will review the already available experimental data and familiarize themselves with the existing literature on bacterial motility and aggregation onset. In collaboration with the experimental collaborators (D. Débarre, LIPhy Grenoble; S. Lecuyer, LPENS Lyon) they will develop a first qualitative understanding of the experimental system at hand and define quantitative measures of individual PA motility and bacteria-bacteria interactions. A wealth of raw experimental data has already been analyzed to extract e.g. bacterial trajectories. Should the Ph.D. candidate wish, they are welcome to contribute to the image analysis of the experiments currently being conducted by the collaborators.
2. Here a minimal microscopic model will be developed to study bacterial aggregation on a solid surface. This microscopic model will be limited to the investigation of the onset of microcolony formation (up to ~100 cells) where bacteria aggregates are present as monolayers on the surface. Thereby the hypothesis will be explored that bacterial aggregation is initiated by MIPS based on a collision-mediated reduction of bacterial speed in regions of high bacterial density. A numerical model based on individual bacteria will be established, that includes key features like substrate-dependent bacterial motility, division, and matrix deposition. If necessary more complex features like long-range cell-to-cell interactions may be included (Gagnieu, 2019). PA motility features are highly dependent on the used strains and surface properties. To benchmark the model we will use already analyzed experimental data sets of bacterial motility and aggregation on various submerged solid surfaces obtained at the LIPhy and the LPENS. Thereby the bacterial motility features are modified by varying the chemical nature or rigidity of the substrate (Gomez, 2023), which mainly affects ballistic velocity, or by varying the topology of the substrate, which affects the persistence length of the bacterial motion (Letrou, 2025).
3. It is already known from continuum modeling that the lateral spreading of biofilms is influenced by physico-chemical effects (wetting, capillarity, substrate rigidity; Pietz, 2025). Here, as a complementary approach to the microscopic model (or possibly as a stand-alone project), a continuum model will be developed to study the early steps of bacterial aggregation, before lateral biofilm spreading sets in. The Ph.D. student will use in particular coarse-graining techniques used in active matter in the context of MIPS (Cates, 2015; Bertin, 2024). The main goal here is to be able to describe larger bacterial assemblies than the ones studied by microscopic numerical simulations, and to identify in a systematic way the key parameters controlling the pattern formation identified in the microscopic model (point 2).

Supervisors: Karin John and Eric Bertin

Research fields: biophysics, soft matter modeling, statistical physics, microscopic and continuous modeling of biological multiagent systems. The project is designed to elucidate the role of physical mechanisms in an experimental biological system. If desired, the Ph.D. may participate in the analysis of experimental raw data (image analysis).

Possible secondments: University of Münster, Germany

Doctoral school: ED PHYS: Physics

Bertin, E. and Solon, A. (2024). Biased motility-induced phase separation: from chemotaxis to traffic jams. J. Stat. Mech.: Theory and Experiment, 2024(5): 053201.

Cates, M. E. and Tailleur, J. (2015). Motility-induced phase separation. Ann. Rev. Cond. Matter Phys. 6: 219.

Flemming H.-C., Wingender J., Szewzyk U., Steinberg P., Rice S.A. and Kjelleberg S. (2016) Biofilms: an emergent form of bacterial life. Nat. Rev. Microbiol. 14: 563.

Gagnieu, A., Chagnon, G., Chemisky, Y., Stéphanou, A. and Chauvière, A. (2019) On the importance of substrate deformations for cell migration. Comput. Methods Biomech. Biomed. Engin. 22: 377.

Gomez, S., Bureau, L., John, K., Chêne, E.-N., Débarre, D., and Lecuyer, S. (2023). Substrate stiffness impacts early biofilm formation by modulating pseudomonas aeruginosa twitching motility. eLife, 12:e81112.

Letrou, M., Encarnacion, K.C., Mathias, R., Carrasco Salas, Y., Gomez Ho, S., Murillo Vilella, E., Bureau, L., Lecuyer, S. and Débarre, D. (2025) Bacterial exploration of solid/liquid interfaces: developing platforms to control the physico-chemical microenvironment. BioRxiv. Doi: 10.1101/2025.07.25.666890.

Pietz, A., John, K. and Thiele, U. (2025) The role of substrate mechanics in osmotic biofilm spreading. Soft Matter 21: 2935.

Desired profile and expected skills

Education, diplomas: The Ph.D. student to be hired has preferentially a background in statistical physics and or biophysics with a strong interest in modeling of biological systems. Basic knowledge of scientific computing is required.

Disciplinary skills, experience: Previous research experience in modeling and scientific programming (C, C++, Python) would be appreciated but is not required.

Personal skills: We seek a highly motivated Ph.D. student with outstanding verbal and written English communication skills and a genuine passion for proactive, interdisciplinary science. Particularly valued is the capacity to critically evaluate simulation results against experimental findings and to develop data driven models. The ideal applicant should be intellectually flexible, willing to harness varied theoretical methodologies, and to process and analyze existing experimental datasets.

General information

This recruitment takes place within the PhD@Tec21 Programme, which is co-funded as part of the Marie Skłodowska-Curie COFUND actions under the grant agreement #101217261. The recruitment process follows a specific selection and evaluation procedure with particular eligibility criteria, all of which are detailed in the applicant guide available on PhD@Tec21 Website.

Employment benefits and conditions

Université Grenoble Alpes (UGA) is offering a 36-month full-time work contract. In line with the European Commission rules for Marie Skłodowska-Curie grant holders, the remuneration will consist of a gross monthly salary of 2,669 EUR. The estimated net salary to be perceived by the PhD fellow will be between 2,050 and 2,152 EUR[1].

Benefits include:

- Access to a high-quality work environment, including a personal computer, scientific equipment and access to library and shared lab facilities
- Full social security benefits and participation to health insurance
- Access to high-level scientific and inter-sectoral training through 120 hours of doctoral courses and workshops
- Opportunity for 2-month secondments at an academic institution or industrial partner during the 2nd year of the PhD
- A vast choice of networking events and activities within the PhD@Tec21 Programme and through the international network of MSCA fellows
- Access to the UGA International Student Office, to assist the PhD fellows in searching for accommodation in Grenoble and support with administrative issues including visas, health, bank accounts, etc.
- Visa fees and registration to the UGA Doctoral School are covered by PhD@Tec21
- Sick leave, parental leave, 45 days of paid holidays

Contact for the questions related to the position:

PhD@Tec21 Management Board:
guillaume.chambon@inrae.fr / amelie.bataille@univ-grenoble-alpes.fr

[1] As an average over the 3 years, depending on French tax regulations. Fellows might benefit from an additional allowance depending on their family situation (74 EUR monthly net allowance)